

REMARKS

This responds to the Office Action mailed on February 2, 2005, and the documents cited therewith. Claims 1, 50, 51, 52, 61, and 63 are amended, claims 31-48, 59 and 60 are cancelled; as a result, claims 1-30, 49-58, 61-64 are now pending in this application. The Examiner is requested to note that the amendment of claim 1 as presented herein does not surrender any equivalent to which the other substituents may be entitled. Accordingly, Applicants are entitled to a full range of equivalents upon issuance of the instant claims. No new subject matter is added.

Affirmation of Election

Restriction to one of the following claims was required:

- I. Claims 1-30, and 49-64 (in part), drawn to a compound of Formula I, their compositions, and methods of use, (when A represents CH) classified in class 546, subclass 157 and class 514, subclass varies.
- II. Claims 31-48 and 49-64 (in part), drawn to a compound of Formula I, their compositions, and methods of use, (when A represents N) classified in class 544, subclass 354 and class 514, subclass varies.

As provisionally elected by Applicants' representative, William F. Prout, on November 12, 2004, Applicants confirm their election to prosecute the invention of Group I, claims 1-30.

The claims of the non-elected invention, claims 31-48, are hereby canceled. Claim 49 is amended to embrace compounds from independent claims 1 (as amended) and 12. However, Applicants reserve the right to later file continuations or divisions having claims directed to the non-elected inventions.

§101 Rejection of the Claims

Claim 60 was rejected under 35 U.S.C. § 101 because the claimed invention is allegedly directed to nonstatutory subject matter. To the extent that this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

This claim has been cancelled. Accordingly, it is respectfully requested that this rejection be withdrawn.

§112 Rejection of the Claims

Claims 59 and 61-64 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking adequate description or enablement. To the extent that this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

Claims 61-64:

Claims 61-64 recite a method of inhibiting cancer in a mammal. An analysis of the Wands factors shows that it would not require undue experimentation to practice the present invention as claimed. (1) *The quantity of experimentation necessary*. When analyzing whether “undue experimentation” is required to practice claimed methods, the key word is “undue” not “experimentation.” *In re Angstadt*, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976). Enablement is not precluded by the necessity for some experimentation, such as performing routine assays. In fact, a considerable amount of experimentation is permissible if the experimentation is merely routine, or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should take. *Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (Bd. App. 1982).

Claims 61-64 recite a method of inhibiting cancer in a mammal. A pharmacological model for the determining the ability of a compound to inhibit cancer cell growth is provided at pages 16-18 of the specification. Applicants submit that these tests can be routinely employed by workers in this field. Thus, it would be improper to maintain that undue experimentation is required for the skilled artisan to test for inhibition of cancer cell growth using such a screen. It is respectfully submitted that screening a claimed compound does not constitute “undue experimentation,” particularly in an art where the skill level is high. *In re Wands*, 8 U.S.P.Q.2d at 1404.

(2) *The amount of direction or guidance presented.* Applicants' specification provides sufficient guidance to allow one of skill in the art to practice the claimed invention. The specification shows a working example at pages 16-18, which provides actual data where tumor cell inhibition was shown. Not only would one skilled in the art understand how to determine if a particular compound inhibits tumor growth, but the specification actually provides an appropriate assay and illustrates the resulting data for representative compounds of the invention against several cancers. The results are described in the specification at pages 18-30 and tabulated in Tables 1-11, at pages 44-54. Furthermore, one skilled in the art, if necessary, can properly look to the state of the art of cancer treatment for useful guidance with respect to screening and determining the inhibitory activities of the claimed compounds. Applicants have therefore provided ample disclosure, with respect to a method of inhibiting cancer cell growth with an effective amount of a compound of formula I, to enable the skilled artisan to practice the invention as claimed. Thus, Applicants respectfully submit that the disclosure, coupled with knowledge in the art at the time the application was filed, would adequately enable one of skill in the art to inhibit cancer cell growth using the claimed compounds.

(3) *The presence or absence of working examples relating to the invention.* The specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation. M.P.E.P. § 2164.02. The specification actually contains guidance for preparing representative compounds and compositions (pages 31-43), including 5 pages of working examples, which illustrate the preparation of representative compounds and 3 pages describing appropriate screening procedures (pages 16-18) for representative compounds. The compounds of the invention have been tested against a known anti-cancer agent, XK469. The data (Tables 1-11, pages 44-54) illustrate that the compounds of the invention have significant inhibitory activity in seven different cell lines. Applicants therefore respectfully submit that the instant specification does contain working examples that clearly demonstrate that cancer cell growth can be inhibited using the claimed methods.

(4) *The nature of the invention* and (5) *The state of the prior art.* The nature of the invention is a method of inhibiting cancer cell growth. Medicinal chemistry and pharmacology are mature fields. Cancer has been known for decades, has been well researched, and a variety

of agents and methods to inhibit cancer cell growth are available. The instant invention thus falls within a well established field. XK469 was reported to have broad activity against transplantable mouse tumors (see page 2, of the specification). Applicants therefore respectfully submit that the state of the prior art is well developed. As a result, one skilled in the art would have access to a body of assays and techniques that could be useful for evaluation of the cancer cell growth inhibiting properties of the recited compounds.

(6) *The relative skill of those in the art.* In the pharmaceutical arts, the typical worker has an advanced degree and often has postdoctoral training. Thus, the relative skill level of those practicing in the art is very high, and screening programs, such as the assays described at pages 16-18 of the specification are considered routine.

(7) *The predictability or unpredictability of the art.* The fact that the outcome of a synthesis/screening program is unpredictable is precisely why a screening program is carried out. The Federal Circuit has explicitly recognized that the need, and methodologies required, to carry out extensive synthesis and screening programs to locate bioactive molecules do not constitute undue experimentation. In re Wands, 8 U.S.P.Q.2d at 1406-1407. Practitioners of the art would be well-equipped to prepare and screen compounds of formula I to identify those compounds that inhibit cancer cell growth. See also, Hybritech Inc. v. Monoclonal Antibodies Inc., 231 U.S.P.Q. 81, 84 (Fed. Cir. 1986) (evidence that screening methods used to identify characteristics [of monoclonal antibodies] were available to the art was convincing of enablement). Thus, the fact a compound of formula I would have to be investigated to determine if it is effective in treating a given cancer, e.g., effective in inhibiting cancer cell growth, does not constitute “undue experimentation” (Ex parte Forman, 230 U.S.P.Q. 546 (Bd. App. 1986)). This is particularly true in an art area where the level of skill is very high and in which the screening of large numbers of compounds has been standard practice for years.

Furthermore, it is submitted that one skilled in the art would not necessarily believe that this is an extremely unpredictable art. The compounds of formula I all possess structurally similar cores. Because of the defined core structures, the data that is presented in the specification, and the inhibitory activity that is shown, Applicant submits that it would be reasonable for one skilled in the art to believe that all of the compounds recited in the claims would possess the recited activity. Additionally, the claims recite ‘an effective amount’, which

is an amount necessary to carry out the claimed effect. Because of this claim element, whether or not there is some unpredictability, claims 60 and 61 exclude any inoperable embodiments.

(8) *The breadth of the claims.* Claim breadth alone does not provide the basis for a nonenablement rejection. In re Moore, 169 U.S.P.Q. 236 (C.C.P.A. 1971). The scope of enablement provided by Applicants need only bear a “reasonable correlation” to the scope of the claims. In re Fisher, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970). Methods for making a compound of formula I are disclosed (page 8, line 28 to page 10, line 24; pages 17-20; and Figures 1-5 of the specification), and Applicants have shown that a representative compound of formula I inhibits cancer cell growth in multiple cell lines (pages 14-16). The claims recite a finite list of compounds, each of which possesses a quinolin-2-yloxy core. The quinolin-2-yloxy core can be substituted at specific cites and the substituents are selected from a reasonable list of variables. The definitions of the varied substituents are not extremely large. Thus, Applicants respectfully submit that the claims are not overly broad.

Conclusion of the claims 61-64 analysis:

The first paragraph of 35 U.S.C. § 112 requires no more than a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of the claims. The above evaluation of the factual considerations outlined by the court in In re Wands demonstrates that the claimed invention can be practiced without undue or unreasonable experimentation. Thus, Applicants respectfully submit that the instant application complies with 35 U.S.C. § 112, first paragraph.

Furthermore, the Examiner has not provided any factual evidence to suggest that the instant specification fails to provide adequate guidance to enable one skilled in the art to practice the claimed invention. Thus, the Examiner has failed to meet the burden required to establish a rejection of the instant claims under §112. Claim 61 recites a straightforward method of inhibiting cancer cell growth, comprising administering to a mammal afflicted with cancer, an amount of a compound of the invention, effective to inhibit the growth of said cancer cells. Claim 61 recites a straightforward method, comprising contacting cancer cells with a recited compound. The specification provides an example of how the method can be practiced. *In vivo* testing against cancer in mice is accepted as a standard test to predict anti-cancer efficacy in

mammals. One of skill in the art would accept that activity against the cancers tested is reasonably predictive of efficacy against the cancers. This is sufficient to meet the requirements of 35 U.S.C. § 112, first paragraph. M.P.E.P. § 2107.02 (I) and (III). The specification further provides information regarding dosages and administration of compounds of the instant invention to animals and mammals that would enable one skilled in the art to practice the claimed method *in vivo* without undue experimentation (page 14, line 26 to page 15, line 9 and Example 7). As discussed above, routine screening is permissible and does not represent undue or unreasonable experimentation. Thus, Applicants respectfully submit that the instant disclosure adequately enables one skilled in the art to practice the claimed invention.

Additionally, it is not the function of the claims to exclude all possibly inoperable embodiments. In re Anderson, 471 F.2d 1237, 176 U.S.P.Q. 331 (C.C.P.A. 1973); Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., 224 U.S.P.Q. 409 (Fed. Cir. 1984); In re Dinh-Nguyen, 181 U.S.P.Q. 46 (C.C.P.A. 1974). Rather, it is the specification that must be evaluated to determine whether or not the specification would enable the art worker to practice the invention without undue experimentation. Ex parte Forman, 230 U.S.P.Q. 546 (B.P.A.I. 1986). As discussed above, the specification provides adequate guidance to one of skill in the art to determine whether or not a compound of formula I inhibits cancer cell growth without undue or unreasonable experimentation. Therefore, Applicants' specification is enabling.

Claim 59 was rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. To the extent that this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

This claim has been cancelled. Accordingly, it is respectfully requested that this rejection be withdrawn.

Allowable Subject Matter

Applicants note with appreciation the Examiner's indication that claims 1-30 are allowable and that claims 49-58 were objected to for containing non-elected subject matter. Claims 49-58 have been amended to remove the overlap of the subject matter from the cancelled

claims. Applicants submit that, in view of the amendments and remarks herein that all claims are in condition for allowance. Thus, it is respectfully requested that the claims pass to issue.

CONCLUSION

Applicants respectfully submit that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (612) 373-6968 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

JEROME P. HORWITZ ET AL.

By their Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 373-6968

Date August 2, 2005

By William F. Prout
William F. Prout
Reg. No. 33,995

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Mail Stop Amendment, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 2 day of August, 2005.

KATE GANNON
Name

Kate G
Signature